

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A cytotoxically active CD3 specific binding construct comprising a first domain specifically binding to human CD3 and an Ig-derived second binding domain,

wherein said first domain is deimmunized and comprises a CDR-H1 region, a CDR-H2 region and a CDR-H3 region, said CDR-H3 region comprising an amino acid sequence as depicted in SEQ ID NO.: 96, 108, 119, 120, 121, 122, 123, 124, 125, 126, or 127; and

wherein said first domain further comprises in its framework H1 the sequence VKK and wherein the transition sequence between framework H1 and CDRH1 region comprises the sequence Ala-Ser-Gly-Tyr-Thr-Phe (ASGYTF; SEQ ID NO.: 233).

2. (Original) The cytotoxically active CD3 specific binding construct of claim 1 further comprising in said first domain a framework H3 comprising the sequence Met-Glu-Leu-Ser (MELS; SEQ ID NO.: 234).

3. (Currently Amended) The cytotoxically active CD3 specific binding construct of claim 1 ~~or 2~~ further comprising in said first domain a framework H3 comprising the sequence Ile-Thr-Thr-Asp-Lys (ITTDK; SEQ ID NO.: 235).

4. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 3~~, wherein said first domain which specifically binds to human CD3 comprises a framework H1 as shown in SEQ ID NO.: 152 or 153.

5. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 4~~, wherein said first domain which specifically binds to human CD3 comprises a framework H2 as shown in SEQ ID NO.: 156 or 157.

6. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 5~~, wherein said first domain which specifically binds to human CD3 comprises a framework H3 as shown in SEQ ID NO.: 160 or 161.

7. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 6~~, wherein said first domain which specifically binds to human CD3 comprises a framework H4 as shown in SEQ ID NO.: 164 or 165.

8. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 7~~, wherein said construct comprises

- (a) a CDR-H1 as depicted in SEQ ID NO.: 88; and
- (b) a CDR-H2 as depicted in SEQ ID NO.: 90 or 92.

9. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 8~~, wherein said construct comprises a V_H-region as depicted in SEQ ID NO.: 74 or 76.

10. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 9~~, wherein said construct comprises a CDR-L1 as depicted in SEQ ID NO.: 98 or 100.

11. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 10~~, wherein said construct comprises a CDR-L2 as depicted in SEQ ID NO.: 102.

12. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 11~~, wherein said construct comprises a CDR-L3 as depicted in SEQ ID NO.: 104.

13. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any one of claims 1 to 12~~ comprising a V_L region in its CD3-specific portion, wherein said V_L region is selected from the group consisting of SEQ ID NO.: 78, SEQ ID NO.: 80, SEQ ID NO.: 82 and SEQ ID NO.: 112.

14. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any of claims 1 to 13~~, wherein said Ig-derived second domain is a scFv.

15. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any of claims 1 to 14~~, wherein said Ig-derived second domain and/or (a) connecting linker-region(s) is/are humanized and/or deimmunized.

16. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any of claims 1 to 15~~, wherein said Ig-derived second domain comprises an antigen-interaction-site with specificity for a cell surface molecule.

17. (Original) The CD3 specific binding construct of claim 16, wherein said cell surface molecule is a tumor specific marker.

18. (Currently Amended) The CD3 specific binding construct of claim 16, ~~any of claims 16 or 17~~, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for a molecule selected from the group consisting of EpCAM, CCR5, CD19, HER-2, HER-2 neu, HER-3, HER-4, EGFR, PSMA, CEA, MUC-1 (mucin), MUC2, MUC3, MUC4, MUC5_{AC}, MUC5_B, MUC7, β hCG, Lewis-Y, CD20, CD33, CD30, ganglioside GD3, 9-O-Acetyl-GD3, GM2, Globo H, fucosyl GM1, Poly SA, GD2, Carboanhydrase IX (MN/CA IX), CD44v6, Sonic Hedgehog (Shh), Wue-1, Plasma Cell Antigen, (membrane-bound) IgE, Melanoma Chondroitin Sulfate Proteoglycan (MCSP), CCR8, TNF-alpha precursor, STEAP, mesothelin, A33 Antigen, Prostate Stem Cell Antigen (PSCA), Ly-6; desmoglein 4, E-cadherin neo-epitope, Fetal Acetylcholine Receptor, CD25, CA19-9 marker, CA-125 marker and Muellierian Inhibitory Substance (MIS) Receptor type II, sTn (sialylated Tn antigen, TAG72), FAP (fibroblast activation antigen), endosialin, EGFRvIII, L6, SAS, CD63, TAG72, TF-antigen, Cora antigen, CD7, CD22, Ig α , Ig β , G250, gp100, MT-MMPs, F19-antigen, CO-29 and EphA2.

19. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any of claims 1 to 18~~, wherein said second Ig-derived binding domain comprises an antigen-interaction site with a specificity for EpCAM.

20. (Original) The CD3 specific binding construct of claim 19, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO.: 31, 33, 35, 37, 39, 49, 55, 58, 61, 63, 65, 67, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323 and 325;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of SEQ ID NO.: 30, 32, 34, 36, 38, 48, 54, 57, 60, 62, 64, 66, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322 and 324; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

21. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any of claims 1 to 18~~, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity CCR5.

22. (Original) The CD3 specific binding construct of claim 21, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO.: 206, 208, 210, 212, 214 or 216;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO.: 205, 207, 209, 211, 213 or 215; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

23. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any of claims 1 to 18~~, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for CD19.

24. (Original) The CD3 specific binding construct of claim 23, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of:

(a) an amino acid sequence as shown in any one of SEQ ID NO.: 190, 192, 194, 196, 198, 200, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407 or 409;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO.: 189, 191, 193, 195, 197, 199, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406 or 408; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

25. (Currently Amended) The CD3 specific binding construct of claim 1, ~~any of claims 1 to 18~~, wherein said Ig-derived second binding domain comprises an antigen-interaction site with a specificity for CD20.

26. (Original) The CD3 specific binding construct of claim 25, wherein said CD3-specific binding construct comprises an amino acid sequence selected from the group of

(a) an amino acid sequence as shown in any one of SEQ ID NO.: 218, 220, 222, 224, 226, or 228;

(b) an amino acid sequence encoded by a nucleic acid sequence as shown in any one of in SEQ ID NO.: 217, 219, 221, 223, 225 or 227; and

(c) an amino acid sequence encoded by a nucleic acid sequence which is degenerate as a result of the genetic code to a nucleotide sequence of (b);

(d) and amino acid sequence encoded by a nucleic acid sequence hybridising with the complementary strand of a nucleic acid sequence as defined in (b) under stringent hybridisation conditions.

27. (Currently Amended) A nucleic acid sequence encoding a CD3 specific binding construct ~~according to~~ of claim 1. ~~any of claims 1 to 26.~~

28. (Currently Amended) A vector comprising a nucleic acid sequence of ~~according to~~ claim 27.

29. (Currently Amended) ~~The vector of claim 28;~~ A vector comprising a nucleic acid sequence of claim 27, which further comprises a nucleic acid sequence which is a regulatory sequence operable linked to said nucleic acid sequence according to claim 27.

30. (Currently Amended) The vector of claim 28 ~~or 29~~, wherein the vector is an expression vector.

31. (Currently Amended) A host transformed or transfected with ~~a vector~~ according to the vector of claim 28. ~~any of claims 28 to 30.~~

32. (Currently Amended) A process for the production of a CD3 specific binding construct of claim 1, ~~according to any of claims 1 to 26~~ said process comprising

culturing a host ~~of claim 31~~ transformed or transfected with a vector comprising a nucleic acid sequence encoding a CD3 specific binding construct of claim 1 under conditions allowing the expression of the polypeptide construct and recovering the produced polypeptide construct from the culture.

33. (Currently Amended) A composition comprising

a) a CD3 specific binding construct of claim 1, or according to any of claims 1 to 26
~~or as produced by the process of claim 32,~~

b) a nucleic acid molecule molecule of claim 27, encoding a CD3 specific binding construct of claim 1, or

c) a vector comprising a nucleic acid sequence encoding a CD3 specific binding construct of claim 1, or of any one of claims 28 to 30

d) a host transformed or transfected with a vector comprising a nucleic acid sequence encoding a CD3 specific binding construct of claim 1, of claim 31

and,

optionally, a proteinaceous compound capable of providing an activation signal for immune effector cells.

34. (Original) The composition of claim 33, which is a pharmaceutical composition further comprising, optionally, suitable formulations of carrier, stabilizers and/or excipients.

35. (Original) The composition of claim 33, which is a diagnostic composition further comprising, optionally, means and methods for detection.

36. (Canceled)

37. (Currently Amended) A method for the prevention, treatment or amelioration of a proliferative disease, a tumorous disease, an inflammatory disease, an immunological

disorder, an autoimmune disease, an infectious disease, viral disease, allergic reactions, parasitic reactions, graft-versus-host diseases or host-versus-graft diseases comprising the administration of a CD3 specific binding construct of claim 1, according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule encoding a CD3 specific binding construct of claim 1, of claim 27, a vector comprising a nucleic acid sequence encoding a CD3 specific binding construct of claim 1, of any one of claims 28 to 30 or a host transformed or transfected with a vector comprising a nucleic acid sequence encoding a CD3 specific binding construct of claim 1 of claim 31 to a subject in need of such a prevention, treatment or amelioration .

38. (Original) The method of claim 37, wherein said subject is a human.

39. (Currently Amended) The method of claim 37, ~~any one of claims 37 or 38~~ further comprising, the administration of a proteinaceous compound capable of providing an activation signal for immune effector cells.

40. (Currently Amended) The method of claim 39, wherein said proteinaceous compound is administered simultaneously or non-simultaneously with [[a]] the CD3 specific binding construct according to any of claims 1 to 26 or as produced by the process of claim 32, [[a]] the nucleic acid molecule of claim 27, [[a]] the vector of any one of claims 28 to 30 or [[a]] the host of claim 31.

41. (Currently Amended) A kit comprising a CD3 specific binding construct of claim 1, according to any of claims 1 to 26 or as produced by the process of claim 32, a nucleic acid molecule encoding a CD3 specific binding construct of claim 1, of claim 27, a vector comprising a nucleic acid sequence encoding a CD3 specific binding construct of claim 1, of any one of claims 28 to 30 or a host transformed or transfected with a vector comprising a nucleic acid sequence encoding a CD3 specific binding construct of claim 1 of claim 31.